

# A BRIEF ORIGINAL CONTRIBUTION

## Alcohol Use and Prostate Cancer Risk in US Blacks and Whites

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Prostate cancer is the most common malignancy in US men (more than 165,000 cases per annum) and occurs substantially more frequently in blacks than in whites. The causes of this disease are, however, poorly understood. Alcohol consumption, which has been clearly related to malignancies of the upper aerodigestive tract, may also increase risk of cancer at other sites, including the prostate. The authors investigated alcohol use as a risk factor for prostate cancer among US blacks and whites. A population-based, case-control study was carried out among 981 men (479 blacks and 502 whites) with pathologically confirmed prostate cancer diagnosed between August 1, 1986, and April 30, 1989, and 1,315 controls (594 blacks and 721 whites) who resided in Atlanta, Georgia; Detroit, Michigan; and 10 counties in New Jersey, geographic areas covered by three population-based cancer registries. In-person interviews elicited information on alcohol use and other factors possibly related to prostate cancer. Compared with never-users, risk for prostate cancer increased with amount of alcohol drunk ( $\chi^2_{\text{trend}}, p < 0.001$ ), with significantly elevated risks seen for those who had 22–56 drinks per week (odds ratio = 1.4; 95% confidence interval 1.0–1.8) and 57 or more drinks per week (odds ratio = 1.9; 95% confidence interval 1.3–2.7). The finding was consistent among blacks ( $\chi^2_{\text{trend}}, p < 0.01$ ) and whites ( $\chi^2_{\text{trend}}, p < 0.05$ ), and among young and old subjects; it was not restricted to a specific type of alcoholic beverage. In this first large study among US blacks and whites, increased risk for prostate cancer was associated with increased alcohol use. The risk was similar for whites and blacks and could not be attributed to tobacco use or to a number of other potential confounders. *Am J Epidemiol* 1996;143:692–7.

alcohol; case-control studies; prostatic neoplasms

Prostate cancer is the most frequently diagnosed cancer in US men, with more than 165,000 new cases annually. Incidence rates of this disease are 27 percent greater and mortality is more than twofold greater in US blacks compared with whites (1). The causes of this disease are poorly understood, as are the reasons for the ethnic difference in occurrence.

Alcoholic beverage consumption has been causally related to malignant tumors of the oral cavity, phar-

ynx, larynx, esophagus, and liver (2), and there is growing, but as yet inconclusive, evidence that it is related to more moderate increases in risk for malignancies at other major organ sites (3, 4), including the prostate (5–7). The common occurrence of prostate cancer implies that even moderately increased risks may have substantial public health significance. Therefore, data from a large population-based, case-control study were used to investigate alcohol consumption as a potential risk factor for prostate cancer among US blacks and whites.

## MATERIALS AND METHODS

### Study design

This case-control study of prostate cancer is one component of a multicenter study of cancers of the esophagus, pancreas, and prostate and of multiple myeloma among US blacks and whites. Study subjects resided in geographic areas covered by the population-based cancer registry of the Georgia Center for Cancer Statistics (Fulton and DeKalb counties), the Metropol-

Received for publication December 18, 1994, and in final form January 31, 1996.

Abbreviations: CI, confidence interval; OR, odds ratio.

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itan Detroit Cancer Surveillance System (Wayne, Oakland, and Macomb counties), and the New Jersey State Cancer Registry (10 New Jersey counties).

### Study eligibility

Cases for this study were men aged 40–79 years, identified from pathology and outpatient records at hospitals covered by these registries, and newly diagnosed with pathologically confirmed prostate cancer between August 1, 1986, and April 30, 1989. Identified cases were included for study on the basis of a study site-, age-, and ethnicity-stratified sampling scheme to ensure representation of both blacks and whites of a broad age range. On the basis of estimated incidence rates and projected participation rates, we planned for 811 case interviews.

Population controls were selected in the three geographic areas proportional to the expected age, sex, and ethnic distribution of the combined cases for the four cancer sites. Controls younger than age 65 years were selected by the Waksberg method of random digit dialing (8); older controls were selected by random sampling from the computerized records of the Health Care Financing Administration. The control interview target was 1,557 subjects.

### Data collection

In-person interviews were conducted for the cases and controls, usually in the subjects' homes. Prostate cancer cases and male controls were questioned about a number of factors, including demographics, occupational history, family history of cancer, dietary intake, and tobacco and alcohol use. Alcohol drinkers were defined as subjects who reported having at least one drink of beer, wine, or liquor per month for at least 6 months. The usual number of drinks per week for each type of alcoholic beverage was derived from questionnaire data on weekday and weekend usual adult consumption. The number of glasses, bottles, and cans of each type of beverage reported by the subject was converted into number of drinks per week, based on the following equivalencies: one drink = 12 ounces (354.8 ml) of beer = 4 ounces (118.3 ml) of wine = 1.5 ounces (44.4 ml) of liquor. Consumption was categorized as light (seven or fewer drinks per week), moderate (8–21 drinks per week), heavy (22–56 drinks per week), and very heavy (57 or more drinks per week). Also collected were the age when drinking started and stopped for each type of alcoholic beverage and the number of years of consumption.

### Statistical analysis

Odds ratios for prostate cancer were estimated by unconditional logistic regression analysis (9), with ad-

justment for age (40–49, 50–54, ..., 70–74, 75 or more years), for study site (Atlanta, Detroit, or New Jersey) and, when appropriate, for ethnicity (black or white). In selected analyses, possible confounding factors were included to assess the independent effect of alcohol use on prostate cancer risk. To test for trend ( $\chi^2_{\text{trend}}$ ), the exposure variable was treated as continuous in the model by entering the median value for each level of the categorical variable among the controls. The population attributable risk was estimated for blacks and whites, with adjustment for age and study site (10) by utilizing weighted estimates to account for the sampling of subjects for inclusion in this study.

### Study subjects

In total, 1,292 cases selected by following the case sampling scheme and 1,767 controls were identified for study. Interviews were obtained for 988 cases (76 percent) and 1,336 controls (76 percent). Among cases, nonparticipation was due to refusal (10 percent), sickness (6 percent), death (4 percent), and other reasons (4 percent) and varied by study site (Atlanta, 23 percent; Detroit, 21 percent; New Jersey, 26 percent). After accounting for nonresponse in the initial phase of screening for eligibility among random digit dialing contacts (screening rate, 86 percent), the response rate for controls was 71 percent (Atlanta, 77 percent; Detroit, 72 percent; New Jersey, 67 percent). Six cases and six controls were dropped from the analysis because of incomplete interviews. Sixteen subjects (one case and 15 controls) were excluded due to a prior history of prostate cancer. The final study group consisted of 981 cases (479 blacks and 502 whites) and 1,315 controls (594 blacks and 721 whites). Fewer than 1 percent of the respondents did not provide information on usual intake of wine, beer, or liquor and were excluded from the relevant analyses.

### RESULTS

The overall risk for prostate cancer associated with consumption of alcohol was only marginally elevated (odds ratio (OR) = 1.2) for both blacks and whites (table 1). Risk increased, however, with amount ( $\chi^2_{\text{trend}}, p < 0.001$ ) and was significantly elevated among both those who had 22–56 drinks per week and those who had 57 or more. The findings were similar among blacks ( $\chi^2_{\text{trend}}, p < 0.01$ ) and whites ( $\chi^2_{\text{trend}}, p < 0.05$ ). Among both blacks and whites, risk associated with alcohol use was similarly increased among both recent (current drinker or quit in the last year) and former consumers of alcohol.

TABLE 1. Alcohol use and prostate cancer risk (odds ratio) by usual amount of alcohol consumed, Atlanta, Georgia; Detroit, Michigan; and New Jersey (10 counties), 1986-1989

Usual alcohol use	Black			White			Total	
	Cases/controls	OR*,†	95% CI*	Cases/controls	OR†	95% CI	OR‡	95% CI
Never used§	94/133	1.0		90/150	1.0		1.0	
Drinks per week								
Any	385/461	1.2	0.9-1.7	412/571	1.2	0.9-1.7	1.2	1.0-1.5
≤7	96/126	1.1	0.8-1.7	136/213	1.1	0.8-1.6	1.1	0.9-1.4
8-21	113/168	1.0	0.7-1.4	140/197	1.2	0.9-1.7	1.1	0.9-1.4
22-56	119/118	1.5	1.0-2.1	92/124	1.2	0.8-1.7	1.4	1.0-1.8
≥57	54/48	1.8	1.1-3.0	42/37	2.0	1.2-3.4	1.9	1.3-2.7
p for trend		<0.01			<0.05		<0.001	
Recent drinker								
≤7	57/78	1.2	0.7-1.9	105/165	1.1	0.8-1.6	1.1	0.8-1.5
8-21	64/105	0.9	0.6-1.4	109/158	1.2	0.8-1.8	1.1	0.8-1.5
22-56	67/73	1.4	0.9-2.2	63/93	1.1	0.7-1.7	1.2	0.9-1.7
≥57	28/28	1.8	0.9-3.3	21/22	1.7	0.9-3.3	1.7	1.1-2.6
Former drinker								
≤7	36/44	1.1	0.6-1.8	28/34	1.3	0.7-2.4	1.2	0.8-1.8
8-21	45/53	1.0	0.6-1.7	29/27	1.6	0.9-2.9	1.3	0.9-1.9
22-56	48/42	1.5	0.9-2.6	29/26	1.7	0.9-3.1	1.6	1.1-2.4
≥57	24/19	1.9	0.9-3.8	20/15	2.2	1.0-4.6	2.0	1.2-3.4

\* OR, odds ratio; CI, confidence interval.

† Adjusted for age and study site.

‡ Adjusted for age, ethnicity, and study site.

§ Referent.

For very heavy consumers of alcohol (57 or more drinks per week), the risk was significantly increased for those who had quit 2-9 years ago (OR = 1.8; 95 percent confidence interval (CI) 1.0-3.4) and those who had quit 10 or more years ago (OR = 2.3; 95 percent CI 1.1-5.0) (data not shown). The pattern of increased risk with increasing alcohol consumption was similar in younger (less than age 65 years) and older men (data not shown), with risk increasing for those who consumed 57 or more drinks per week, to odds ratios of 2.1 (95 percent CI 1.3-3.4) and 1.7 (95 percent CI 1.0-2.9) for younger and older men, respectively.

Increased risk was most clearly evident in association with moderate and poorly differentiated or undifferentiated tumors (table 2). Among heavy drinkers (57 or more drinks per week), risk for advanced grade tumors (moderate, poor, and undifferentiated) was increased among blacks (OR = 2.0; 95 percent CI 1.1-3.6) and whites (OR = 2.1; 95 percent CI 1.1-3.8) (data not shown). Differences in risk by stage of disease, however, were less evident.

The pattern of increased risk with increased consumption was apparent for beer ( $\chi^2_{\text{trend}}, p < 0.001$ ) and liquor ( $\chi^2_{\text{trend}}, p < 0.001$ ), but not for wine (table

TABLE 2. Alcohol use and risk (odds ratio\*) of prostate cancer by tumor grade and stage, Atlanta, Georgia; Detroit, Michigan; and New Jersey (10 counties), 1986-1989

Drinks per week	Tumor grade									Tumor stage					
	Well differentiated			Moderate			Poor/undifferentiated			Localized			Regional/distant		
	Cases	OR†	95% CI†	Cases	OR	95% CI	Cases	OR	95% CI	Cases	OR	95% CI	Cases	OR	95% CI
None‡	59	1.0		64	1.0		46	1.0		112	1.0		56	1.0	
≤7	70	1.0	0.7-1.5	88	1.2	0.8-1.8	52	1.0	0.7-1.6	149	1.2	0.9-1.6	65	1.0	0.7-1.5
8-21	82	1.1	0.7-1.5	79	1.0	0.7-1.4	63	1.1	0.7-1.6	144	1.0	0.8-1.4	84	1.1	0.8-1.7
22-56	62	1.2	0.8-1.8	70	1.3	0.9-1.9	50	1.3	0.8-2.0	124	1.3	1.0-1.8	63	1.3	0.9-1.9
≥57	25	1.4	0.8-2.4	33	1.9	1.1-3.1	27	2.1	1.2-3.6	52	1.7	1.1-2.6	36	2.1	1.3-3.5

\* Adjusted for age, ethnicity, and study site.

† OR, odds ratio; CI, confidence interval.

‡ Referent.

3). The association for beer was stronger in blacks and that for liquor in whites. Further analyses comparing drinking patterns for each beverage type, adjusting for the consumption of the other types, showed similar results.

In this study, no clear association for prostate cancer was seen with amount of tobacco use (11). The pattern of increasing risk with increasing alcohol consumption is also apparent in each subgroup defined by increasing tobacco use (1-19, 20-39, and 40 or more pack-years). In addition, the association of alcohol use with prostate cancer was substantively unchanged by statistical adjustment for other potential confounders that included education, income, body mass index, nonalcohol caloric intake, fat intake, fruit and vegetable consumption, history of liver cirrhosis, and family history of prostate cancer.

The population attributable risk for prostate cancer associated with alcohol consumption was 14 percent for blacks and 15 percent for whites. The attributable risks associated with consumption of 22-56 drinks per week were 8 and 3 percent and those associated with consumption of 57 or more drinks per week were 5 and 4 percent for blacks and whites, respectively.

## DISCUSSION

Our results provide the first evidence of a dose-response relation between alcoholic beverage consumption and risk of prostate cancer. Risk was similarly elevated in US blacks and whites. The population attributable risk, taking the prevalence of alcohol consumption and the associated relative risks into account, was also similar for the two ethnic groups. Risk was more clearly evident for prostate cancer of advanced grade, but results were similar by disease stage. Risk of prostate cancer was elevated regardless of the type of alcoholic beverage consumed, suggesting that the association is due to alcohol, not to some components of specific types of beverages. Nor did the association appear to be connected with tobacco use, history of cirrhosis, or a number of other potential confounders. Risk did not decrease with discontinuance of alcohol use, which implies that alcohol may be associated with early events in the development of this disease.

Although alcohol has not generally been considered a risk factor for prostate cancer (2), our study suggests otherwise. Significantly increased risks of prostate

TABLE 3. Alcohol use and prostate cancer risk (odds ratio) by type of alcoholic beverage, Atlanta, Georgia; Detroit, Michigan; and New Jersey (10 counties), 1986-1989

Usual alcohol use	Black			White			Total	
	Cases/controls	OR*,†	95% CI*	Cases/controls	OR†	95% CI	OR‡	95% CI
Never used§	94/133	1.0		90/150	1.0		1.0	
Drinks of beer per week								
≤7	137/191	1.1	0.8-1.5	169/242	1.2	0.9-1.7	1.2	0.9-1.5
8-14	55/78	1.0	0.6-1.5	75/96	1.3	0.9-2.0	1.2	0.9-1.6
15-28	55/54	1.5	0.9-2.4	50/64	1.3	0.8-2.1	1.4	1.0-2.0
≥29	33/22	2.7	1.4-5.2	51/48	2.0	1.2-3.2	2.1	1.4-3.1
p for trend		<0.01			<0.05		<0.001	
Drinks of wine per week								
<3	40/47	1.3	0.8-2.2	90/117	1.4	1.0-2.1	1.4	1.0-1.9
3-14	36/39	1.4	0.8-2.4	60/95	1.1	0.7-1.7	1.2	0.8-1.6
>14	23/19	2.1	1.0-4.3	21/34	1.2	0.6-2.2	1.4	0.9-2.2
p for trend		0.05			0.97		0.28	
Drinks of liquor per week								
≤7	111/134	1.2	0.8-1.8	178/248	1.2	0.9-1.7	1.2	0.9-1.6
8-14	77/95	1.2	0.8-1.8	54/78	1.2	0.7-1.8	1.2	0.9-1.6
15-28	68/81	1.2	0.8-1.8	50/64	1.3	0.8-2.2	1.3	0.9-1.8
≥29	71/66	1.6	1.0-2.5	51/48	2.6	1.4-4.8	1.9	1.4-2.7
p for trend		0.07			<0.01		<0.001	

\* OR, odds ratio; CI, confidence interval.

† Adjusted for age and study site.

‡ Adjusted for age, ethnicity, and study site.

§ Referent.

cancer have been shown in a large cohort of alcoholics from Denmark (6) and among alcoholics from Sweden who were less than age 65 years, but not among those who were age 65 or older (7). In addition, a large Japanese census-based cohort study (5) reported an excess of prostate cancer among men who were daily drinkers of strong liquor. An Italian case-control study (12) that included substantial numbers of heavy drinkers of wine did not show an excess risk, and studies with smaller numbers of heavy drinkers of alcohol showed either weak or no association between alcohol use and prostate cancer (13-20).

Although the mechanisms of alcohol-related carcinogenesis are unclear, it is plausible that alcohol may play a role in prostate carcinogenesis. As diet probably plays a role in prostate cancer (21), alcohol consumption might be related to prostate cancer indirectly through dietary effects, including nutrient displacement, malabsorption, and liver effects and related pathology (22). Early autopsy studies (23, 24), however, found a lower prevalence of prostate cancer in cirrhotics than in controls, suggesting that physiologic changes associated with cirrhosis may reduce prostate cancer risk. Given the prevalence of occult prostate cancer found on autopsy, these early findings should be reexamined with attention to pathologic characterization of grade and stage.

Alcohol might also affect prostate cancer directly, since alcohol contains congeners and other contaminants that may be carcinogenic (2). Its major metabolite, acetaldehyde, is a recognized animal carcinogen and teratogen (25), and some other products of alcohol metabolism may have hormone-related toxic effects (26). Alcohol could also affect the metabolism of carcinogens through its influence on cytochrome P450 and other enzymes (27-29), as illustrated by ethanol-enhanced tumorigenesis by nitrosamines in rodents (30, 31). The extent to which alcohol and its products are metabolized in the prostate is unknown, but aldehyde dehydrogenases have a physiologic role in the detoxification of prostatic oxidation products of the biogenic polyamines, putrescine, spermidine, and spermine (32), which are produced in large quantities there. Acetaldehyde products of alcohol ingestion could act as a competitive substrate to this detoxification process. Alcohol is known to influence hormone levels (27, 33-36), even in utero (37), and has been shown to influence hormone-related carcinogenesis (38).

Underreporting is common in interview studies of alcohol consumption (39) and could have biased our result if study controls underreported alcohol use to a greater extent than did the prostate cancer cases. Because information on subjects with cancers of the

esophagus and pancreas and multiple myeloma was also collected as part of this study, we could assess the relation of alcohol use to cancer at these sites. There was a strong association with esophageal cancer in both blacks and whites (40), a moderate association with pancreatic cancer (in some subgroups) (unpublished data), and no association with multiple myeloma (unpublished data). The lack of an association with multiple myeloma, a disease not connected to alcohol use, supports the assumption that our results for prostate cancer were not caused by differential underreporting of alcohol use by the controls. This observation is further supported by comparison with survey data on alcohol consumption patterns among US men (41), who report less alcohol use than is indicated here for our control group.

In summary, we found that prostate cancer increased with increased consumption of alcohol. The risk was similar for whites and blacks and could not be attributed to tobacco use or to a number of other potential confounders. Our study was unique in its large sample size, which included substantial numbers of heavy drinkers, but the observed associations will need to be confirmed in studies of similar scale.

#### ACKNOWLEDGMENTS

The study was funded in part through National Cancer Institute contracts to the Michigan Cancer Foundation (NO1-CP-5109, NO1-CN-05225), the New Jersey State Department of Health (NO1-CP-51089, NO1-CN-31022), the Georgia Center for Cancer Statistics (NO1-CP-51092, NO1-CN-05227), and Westat, Inc. (NO1-CP-51087).

The authors thank Ruth Thomson of Westat, Inc., for her assistance in study management and coordination; Roy VanDusen of Information Management Systems for computer support; and the interviewers, support staff, physicians, and hospital personnel in the study areas for their participation.

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